Claims 17, 18, 23 and 24 were rejected under 35 U.S.C.§112 as being indefinite. Applicants respectfully traverse this rejection.

Claims 17 and 18 were said to be vague in their recitation of "A pharmaceutical composition". Applicants respectfully traverse. A "pharmaceutical composition" is intended to have its ordinary art-understood meaning, i.e. a composition of matter which is intended for a pharmaceutical use. As such it may have a pharmaceutically acceptable carrier and/or other elements. The specification at the paragraph spanning pages 3-4 is clear and provides sufficient guidance for interpretation of these claims. Therefore, it is respectfully requested that these rejections be withdrawn.

Claim 23 was rejected for containing a repetition of the phrase "the L1 protein". Applicants have amended this claim, therefore it is respectfully requested that this rejection be withdrawn.

Claim 24 was rejected as being a duplicate of Claim 13. Applicants respectfully traverse this rejection. Claim 13 defines a protein as being encoded by a particular DNA sequence. Claim 24 defines a protein as a function of its amino acid sequence. While the amino acid sequence of SEQ.ID.NO. 2 is coded for by the DNA of SEQ.ID.NO: 1, due to the redundancy of the genetic code there are numerous DNA sequences which can code for the amino acid sequence of SEQ. ID. No: 2. All these variations are intended to be encompassed in Claim 24. As Claims 24 and 13 do not have the same scope, they are not duplicates of each other, it is respectfully requested that this rejection be removed.

Claims 15-20 were rejected under 35 U.S.C. §112. It was alleged that the specification does not provide any guidance to one of ordinary skill in the art how to make a vaccine or how one would

prevent disease using the sequences provided. Applicants respectfully traverse this rejection.

The specification adequately teaches one of ordinary skill in the art how to make and use a vaccine using the claimed sequences. At this time, there are no FDA approved HPV vaccines. However, there is no requirement in the law that a pharmaceutical use be exemplified with clinical trials proving safety and efficacy. In the instant case, the Applicants' specification teaches on of ordinary skill in the art how to make and use an HPV18 vaccine. In the paragraph spanning pages 2-3, the specification explains how cottontail rabbit papilloma virus (CRPV) and bovine papilloma virus animal models are considered acceptable models for disease. In these models, the L1 and L2 HPV proteins have been identified as good targets for immunoprophylaxis, as animals have been immunized using these proteins. There is no evidence offered which would suggest to one of ordinary skill in the art that the HPV18 L1 protein would not be such a target.

As to the formulation of the protein into a vaccine, the art has many recognized techniques, which are noted in the specification along with recognized references (see page 4, lines 1-6). Dose ranges have been provided along with various methods of administration (page 4, lines 8-35). Thus, contrary to the assertions in the Office Action, Applicants have taught one how to adequately make and use their invention and have enabled all claims. Therefore, it is respectfully requested that this rejection be removed.

Claims 13-24 were rejected under 35 U.S.C.§103 as obvious over Lowy et al ("Lowy"), Kirnbauer et al ("Kirnbauer") and Rose et al ("Rose"). Lowy is cited for teaching production of HPV16 in yeast and insect host cells, purification and vaccine development. Rose is cited for teaching production of HPV18 in yeast. Kirnbauer is cited for teaching the isolation of HPV16 from a condylomata acuminata,

and its subsequent cloning. It is argued that the combination of the three references would result in Applicants' invention, as it would be obvious to substitute HPV18 for the HPV16. Applicants respectfully traverse this rejection.

The nucleic acid and amino acid sequences for Applicants' claimed HPV18 are different from those in the art. Rose (see Example X, page 27) uses nucleic acid from the "HPV-18 prototype" virus. This is the HPV-18 virus which is described in Cole et al, 1987 "Nucleotide Sequence and Comparative Analysis of the Human Papillomavirus Type 18 Genome" *J. Mol. Biol.* 193:599-608 (submitted previously). The sequences which Applicants are claiming differ from this sequence as described in Example 5 (pages 19- 20) and detailed in Table 2.

Applicants' DNA sequence has 20 base pair changes out of 1524 nucleotides. Five nucleotide changes result in amino acid changes. Applicants' sequence is a consensus sequence from clinical isolates, and thus antibodies which are produced as a result of exposure to this vaccine will be more specific against the clinical forms of the virus, since the antigen is more akin to the clinical antigen.

The three cited publications are silent as to the fact that the published HPV18 L1 sequence differs significantly from sequences which are found in clinical strains of the HPV18 virus. There is no motivation in any of the cited references for a researcher to investigate any further source of HPV18 other than Rose "prototype HPV18", as there is no indication that alternate forms of HPV 18 L1 even exist. Thus, given the combination of the three cited references, one of ordinary skill in the art would not have possession of Applicants' invention, as the claimed sequences are not taught nor suggested. Therefore, one must conclude that there is no obviousness and it is respectfully requested that this rejection be withdrawn.

Applicants maintain that all claims are in condition for allowance and a favorable action on the merits is earnestly solicited.

Respectfully submitted,

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